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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,763	10/26/2001	Ronald P. Taylor	9426-059	4486

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EXAMINER	
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ART UNIT	PAPER NUMBER
1644	
MAIL DATE	DELIVERY MODE
03/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/016,763	TAYLOR ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6,8-17 and 20-22* is/are pending in the application.

4a) Of the above claim(s) *6,8-17 and 20-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation of U.S. Application Serial Number 08/202,572.

Claims 2, 5, 7, and 18-19 have been canceled.

Claims 1, 3, 4, 6, 8-17 and 20-22 are currently pending.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 31, 2007 has been entered.

Election/Restrictions

2. **Claims 6, 8-17 stand withdrawn** from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on April 7, 2006.

Newly added claim 20 is dependent on and reads on non-elected claim 6. Newly added claim 21 is dependent on and reads on non-elected claim 14. **Claims 20-22 do not read upon the elected invention and are therefore also withdrawn.**

Accordingly, **claims 1, 3 and 4 remain the subject of examination** in the present Office Action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly

owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1, 3 and 4 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Taylor et al (J. Immunol. [1992] 148(8):2462-2468; C17 on form PTO-1449 filed 12/23/04) in view of Kimberly et al (J. Clin. Invest. [1989] 84(3):962-970; C10 on form PTO-1449) and Emlen et al (J. Immunol. Meth. [1990] 132(1):91-101; C03 on form PTO-1449).

It was previously stated: "Taylor teaches the production of bispecific heteropolymers comprising an antibody to complement receptor (CR1) on primate erythrocytes. Taylor specifically teaches the monoclonal antibody 1B4 [claim 2] as a part of the heteropolymer (page 2462, column 2 in particular). Taylor teaches conjugation of 1B4 via avidin/biotin linkage to a second antibody, which is directed to an antigen of interest. Taylor further teaches the usefulness of the heteropolymer for erythrocyte-mediated clearance immune complexes in a primate (squirrel monkey) subject (Abstract in particular).

Taylor does not teach heteropolymers of anti-CR1 antibodies with an antigen that is specifically recognized by a pathogenic antibody or autoantibody.

Kimberly teaches erythrocyte-mediated clearance of dsDNA/anti-dsDNA immune complexes (Abstract in particular). Kimberly further teaches that these immune complexes "are relevant to autoimmune disease," "have well characterized immunochemical properties" and their behavior has been studied in primates. Kimberly further teaches that the immune complexes fix complement efficiently, bind avidly to primate erythrocytes via CR1 and release slowly from human erythrocytes (page 967, column 1 in particular). Accordingly, Kimberly establishes the importance of dsDNA/anti-dsDNA complexes in autoimmunity, providing motivation for a person having ordinary skill in the art at the time the invention was made to identify methods of removing the pathogenic anti-dsDNA antibodies.

The teachings of Taylor and Kimberly do not specifically teach heteropolymers comprising anti-CR1 monoclonal antibodies and dsDNA.

Emlen teaches methods for biotinylating dsDNA in a manner suitable for attaching the biotinylated dsDNA to streptavidin. Emlen further teaches that the biotinylated dsDNA retains its immunogenicity (Abstract in particular). Accordingly, the artisan would reasonably expect that biotinylated dsDNA would be able to be bound by anti-dsDNA antibodies in the peripheral circulation of a subject having an autoimmune disease in which anti-dsDNA antibodies are a factor.

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings in order to facilitate erythrocyte-mediated removal of anti-dsDNA antibodies from the peripheral blood of primates with an autoimmune disease such as systemic lupus erythematosus (SLE). One would have been motivated to combine the teachings with a reasonable expectation of success because Taylor teaches that the use of an anti-CR1 antibody such as 1B4 would be an effective way to facilitate erythrocyte-mediated clearance of immune complexes from primates, Kimberly teaches that dsDNA/anti-dsDNA immune complexes can be cleared from a primate via erythrocyte-mediated clearance and Emlen teaches that biotinylated dsDNA retains its ability to bind pathogenic anti-dsDNA antibodies from the blood of subjects with SLE. Therefore the artisan would have reasonably expected that replacing the biotinylated second antibody of the complex taught by Taylor with the biotinylated dsDNA of Emlen would create a complex comprising an anti-CR1 antibody and an antigen specific for an a target pathogenic antibody or autoantibody that is useful for facilitating erythrocyte-mediated removal of the target pathogenic antibody or autoantibody.

Applicant's arguments filed December 14, 2007 have been fully considered but they are not persuasive.

Applicant argues that the references cannot be combined because there is no suggestion in any of the references that they could be combined with any of the other references. Applicant asserts that Taylor requires that the Fc portion of the second antibody is present. However, applicant has not pointed out where in the teaching that this "requirement" is made, nor can such a requirement be found. The anti-CR1 antibody and the anti-pathogen antibody of the construct taught by Taylor are joined an avidin-biotin linker. When one skilled in the art looks at the teaching in its totality, the artisan would recognize that any molecule that is useful for the removal of a pathogenic molecule from a subject's body that can be attached to biotin can be linked to the anti-CR1 antibodies for enhanced clearance of the pathogenic molecule from the body. Kimberly teaches the pathogenicity of dsDNA/anti-dsDNA immune complexes in autoimmunity. Emlen teaches that dsDNA can be biotinylated and attached to streptavidin, but retains its immunogenicity to anti-dsDNA antibodies. Accordingly, the artisan taking these teachings in their totality would recognize that biotinylated dsDNA can be attached via an avidin or streptavidin bridge to biotinylated anti-CR1 antibodies in order to enhance the clearance of the pathogenic anti-dsDNA antibodies from the subject."

Applicant's arguments filed December 14, 2007 have been fully considered but they are not persuasive.

Applicant's quotation of prior case law to set up the arguments regarding the non-obviousness of the claims is noted. However, it is also noted that Applicant has omitted portions of the case law citations of *In re* Vaeck and *In re* Dow in a manner that changes the meaning of the quotation. Applicant is reminded that in *In re* Vaeck the Court also stated that the expectation need only be a reasonable one and not absolute predictability. In other words, the references do not need to predict the outcome of the combination, but the artisan need only have a "reasonable expectation of success" in combining the teachings. Also, Applicant omitted the word "founded" in the citation of *In re* Dow, which properly reads, "Both the suggestion and the expectation of success must be **founded** in the prior art (emphasis added)." Applicant's version implies that the suggestion and expectation must both be physically recited in the prior art. The term "founded" refers to a foundation, meaning not only what is explicitly stated in the references, but also what would be in the knowledge base of the practitioner of the art.

Applicant argues against the combination by focusing on elements that each particular reference does not teach. Applicant argues that Taylor teaches away from the combination because of the requirement for an Fc portion of a second antibody that is not bound to CR1 for clearance of the complex. Applicant has pointed out the citation in the Taylor reference that puts forward this concept. Applicant argues therefore that a complex made by the combination of Taylor, Kimberly and Emlen would not be functional for the clearance of immune complexes. The examiner disagrees. The claims are drawn to the heteropolymer, which can be made by the combination of references set forth here. The question then, is "would that complex provide the practitioner with a 'reasonable expectation of success' in the use of that

complex in order to motivate that artisan to make the combination, even in light of Taylor's teaching that a non-CR1-bound antibody having an FC region may be required for clearance of the immune complex?" It is submitted that the answer to this question is "yes." The heteropolymer that would be made by the combination of the references comprises an antigenic target molecule that is specifically bound by a pathogenic anti-dsDNA antibody. The pathogenic anti-dsDNA antibodies found in the circulation of a subject with SLE are whole antibodies. The antigen binding site of the antibody would bind to the dsDNA of the heteropolymer, leaving the Fc portion of the pathogenic antibody free. Accordingly, the pathogenic antibody would provide the Fc portion of a second antibody that is not bound to CR1 to satisfy the asserted requirement for clearance of the complex. Therefore, the artisan would reasonably expect that the heteropolymer made by the combination of references would be function for the clearance of immune complexes comprising heteropolymers and pathogenic antibodies bound thereto.

Conclusion

4. No claim is allowed.

5. This is a continued examination of applicant's earlier Application No. 10/016,763. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571)272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

F. Pierre VanderVegt, Ph.D. /PV/
Patent Examiner
March 15, 2008

/David A Saunders/
Primary Examiner, Art Unit 1644